REMARKS

Claims 1, 3, 4, 6-11, 13, 14, 16-24, 26-31, 33, 34, and 36- 42 are pending. Claims 43-50, which were withdrawn from consideration as a result of a restriction requirement, are cancelled without prejudice to the prosecution of their subject matter in other patent applications. Claims 2, 5, 12, 15, 25, 32 and 35 are cancelled without prejudice as redundant in view of amendments made to the claims. The claims are amended herein without prejudice to the prosecution of subject matter cancelled by amendment in other patent applications, and none of the amendments constitute new matter.

The claims are rejected under the first and second paragraphs of 35 U.S.C. §112. For reasons set forth herein, the rejections should be removed and the claims should be deemed allowable.

1. The Claims Are Clear And Distinct

Claims 5-9, 15-19, 25-29 and 35-39 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, claims 5, 15, 25 and 35 are rejected for reciting "for example" and their dependent claims are rejected for the same reason.

Claims 5, 15, 25 and 35 are deleted, thereby obviating the basis for this rejection, which should be withdrawn.

2. **Claims 1-40 Are Enabled**

Claims 1-40 are rejected under 35 U.S.C. §112, first paragraph, as unenabled. The Examiner states:

> The instant claims are drawn to methods of inhibiting proliferation and/or inducing apoptosis in cancer cells by increasing the amount of MDA-7 and decreasing the activity of RAS in the cancer cells (e.g., see claims 1, 21, 31). The claimed methods, however, do not set forth any method steps for completing BOTH increasing the amount of MDA-7 and decreasing RAS activity in cancer cells. Therefore, applicants have not adequately indicated how to make/use the invention.

As an example, the Examiner cites claim 9, which provides for a method of decreasing the activity of RAS but not a method for increasing the amount of MDA-7. The Examiner states that "amending the claims to clearly indicate the steps by which both increasing MDA-7 and decreasing RAS activity is achieved would obviate this rejection."

Applicant has amended the claims to recite specific methods that may be used to increase the amount of *MDA*-7 and decrease *RAS* activity, thereby obviating the basis for the rejection, which should be withdrawn.

3. **The Claims Satisfy the Written Description Requirement And Are Enabled**

Claims 1-42 are rejected under 35 U.S.C. §112 as failing to meet the written description requirement. The Examiner states:

> The instant claims are drawn to method of inhibiting proliferation of cancer cells by increasing the amount of MDA-7 and decreasing the activity of RAS in the cancer cells (e.g., see claims 1, 21, 31). It is noted that the claims are very broad and encompass any molecules that increase MDA-7 and any molecule that decreases RAS activity in a cell. Furthermore, claims 1-40 encompass any molecules that can increase MDA-7 as well as decrease RAS activity in a cell. Considering the breadth of the claims, the claims encompass a genus of molecules

> indefinite in size, but which may possibly encompass possibly thousands of different molecules, considering every molecule that could possibly directly, or even indirectly, increase MDA-7 and/or decrease RAS activity in a cell.
> and
> . . . considering the breadth of the claims and the limited number of species disclosed, the specification has not adequately described the genus encompassed by the claims. For instance, the specification has not described any molecules that can BOTH increase MDA-7 and decrease RAS activity in a cell. Furthermore, considering the claims encompass molecules which have not yet been identified including molecules which have unrelated chemical structures and biological functions, the few species disclosed is not representative of the entire genus encompassed by the claims.

The Examiner also contends that claims referring to the use of antisense molecules would encompass any antisense molecule with an anti-*RAS* effect.

Finally, the Examiner concludes that in view of the written description rejection, the claims are not enabled, so that they are further rejected under the enablement section of the statute.

In response, Applicant respectfully asserts that the claims satisfy the written description and enablement requirements. As set forth above, the claims have been amended to more particularly recite molecules that may be used to produce the two desired effects of the present invention, namely increasing levels of *MDA*-7 protein or inhibiting *RAS* activity. With regard to the Examiner's contention that the claims would encompass any antisense molecule having an anti-*RAS* effect, the claims have been amended to more particularly refer to "antisense *ras* molecules," as described in page 30 paragraph 63 of the specification.

For these reasons, the rejection for lack of written description and the related rejection for lack of enablement should be withdrawn.

4. Claims 1-42 Are Enabled

Claims 1-42 are rejected under 35 U.S.C. §112, first paragraph, as unenabled. The Examiner contends that while the specification enables a claim directed to:

> A method for inhibiting proliferation and/or inducing apoptosis in pancreatic cancer cells expressing K-ras by directly administering to said pancreatic cancer cells a composition comprising (i) a nucleic acid that encodes and expresses MDA-7 in cancer cells and (ii) an antisense nucleic acid molecule that specifically hybridizes to a nucleic acid encoding K-ras under stringent conditions

it does not, according to the Examiner, enable the full scope of the claims. The Examiner concludes that:

> [c]onsidering the breadth of the claims, the high degree of unpredictability of gene therapy recognized in the art, the limited working examples and guidance in the specification, and the high degree of skill required, . . . the amount of experimentation required to perform the broadly claimed invention is undue.

As set forth above, the claims are amended to more particularly identify molecules that may be used to effect the required increase in *MDA-7* and molecules that inhibit *RAS* activity. The obtention of such recited molecules is within the skill in the art, and the use of combinations of such molecules to increase *MDA*-7 and inhibit *RAS* activity may be achieved using routine experimentation.

In addition, Applicant has, in order to advance the prosecution of this application and without prejudice, amended the claims to pertain to preferred embodiments of the invention in which the cells to be treated contain a mutated *ras* gene which results in increased *RAS* activity (as set forth in the instant specification at page 36 paragraph 78). This comports with the working example contained in the application,

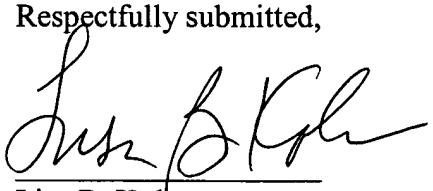
which shows that "the synergistic effect of *MDA-7* and *ras* antisense molecules is observed in pancreatic cancer cells having a mutation activated *ras* gene, but not in cells having wild-type *ras*" (in the instant specification at page 36 paragraph 77). An activating mutation of *RAS* has been associated with a number of malignancies, as listed in paragraph 78 of the instant specification. The amended claims therefore capture the functional relationship wherein an increase in *RAS* activity in the context of malignant cells is addressed by *RAS* inhibitors (such as antisense *ras* molecules) *in combination with* increased levels of *MDA*-7 protein.

It is therefore asserted that the claims are enabled and accordingly, it is requested that the rejection be withdrawn.

5. Conclusion

For all the foregoing reasons, it is respectfully requested that the rejections of the claims be withdrawn. An early allowance is earnestly requested.

Respectfully submitted,



Lisa B. Kole
Reg. No. 35,225
(212) 408-2628

BAKER BOTTS L.L.P.
Attorneys for Applicant